REMARKS/ARGUMENTS

Claims 14-25 are active in this case. Support for these claims is found in original Claims 1-13 (now cancelled) and the specification on pages 8-9. Claims 14-25 are directed to the elected subject matter, previously identified as Group I.

The specification is amended to provide a cross-reference to related applications.

No new matter is believed to have been added by the addition of these amendments.

The rejection of Claims 1-13 under 35 USC 112, second paragraph is no longer applicable in light of the cancellation of these claims. Moreover, the issues raised in the Office Action are not applicable to the new claims presented herein. Specifically, the phrase "transgenically introduced," unnecessary or detrimental," "genes associated with . . . ," "causing a transformant ... extrinsic to the host," are not present in the claims.

The claims as set forth herein are to constructing a yeast cell and/or producing a heterologous protein with the yeast cell, in which certain specified genes are deleted or inactivated and the resultant yeast cell is used to produce a heterologous protein.

Accordingly, withdrawal of this rejection is requested.

The rejection of Claims 1-13 under 35 USC 112, first paragraph is no longer applicable in light of the cancellation of these claims. Moreover, the issues raised in the Office Action are not applicable to the new claims presented herein.

As is clear in the claims as submitted, the yeast cell is limited to *S. pombe*, the specific genes deleted or inactivated are listed, which in turn increases expression of a heterologous protein. As discussed in the specification on pages 3-4 and 8-9, the inventors have found that by deleting or inactivating certain genes in *S. pombe*, they were able to boost protein expression markedly. While the Examples utilize a GFP marker protein as a simple model to

show how their invention works, as the Examiner will appreciate, GFP is simply a model and once one has the modified yeast strain in hand, he/she can certainly transform that yeast cell with a heterologous polynucleotide sequence encoding a protein. Thus, the limitation to certain yeast cells coupled with the specific genes deleted or inactivated, as set forth on page 8-9 of the specification, demonstrates quite clearly that Applicants had possession of the invention as claimed herein.

Withdrawal of this rejection is requested.

The rejection of Claims 1-13 under 35 USC 102(b) in view of US patent no. 6,110,703 ("Egel-Mitani") is no longer applicable in light of the cancellation of the rejected claims. Moreover, the Egel-Mitani patent does not describe the methods as claimed herein. Specifically, this patent describe deleting a YAP3 protease, which as stated in col. 2, lines 19-20 of the patent is a protease which cleaves arginine residues. What Egel-Mitani does not describe is the deletion of at least one gene chosen from pyruvate decarboxylase, aspartic protease, serine protease, aminopeptidase, and carboxypeptidase as set forth in the claims. Therefore, the claims are not anticipated by the disclosure of this patent and as such withdrawal of this rejection is requested.

The rejection of Claims 1-13 under 35 USC 102(b) in view of the Simeon publication is no longer applicable in light of the cancellation of the rejected claims. Moreover, Simeon does not describe the methods as claimed herein. Specifically, the Simeon publication is concerned with the characterization of the CPY^{SC} gene of *S. cerevisiae* in *S. pombe*. As discussed on page 271, second column, this gene encodes a serine exopeptidase. To do this, Simeon constructed a mutant *S. pombe* strain to obtain a CPY mutant. Then, the *S. cerevisiae* gene is introduced into this mutant stain and characterized. There is no discussion to

specifically mutate at least one of a pyruvate decarboxylase, aspartic protease, serine protease, aminopeptidase, and carboxypeptidase and to express a heterologous protein at increased levels as claimed. In fact, contrary to the conclusion on page 17-18 of the Official Action, the expression of the *S. cerevisiae* gene in the mutant *S. pombe* strain does not inherently result in increased expression. Rather the data in Simeon itself makes clear that this is not the case. Specifically, on page 276, Table 2, Simeon presents enzymatic activity of the CPY enzyme from wildtype *S. cerevisiae* and *S. pombe* (1.45 and 1.25 mU/mg) in relation to the mutant *S. pombe* containing the *S. cerevisiae* gene (Yep13/PRC1) which yielded activity less than either wildtype strain (0.80 mU/mg).

Accordingly, withdrawal of this rejection is requested.

The rejection of Claims 1-9 under 35 USC 102(b) in view of Sharma et al is no longer applicable in light of the cancellation of these claims. Moreover, the Sharma publication does not describe the methods as claimed herein. Specifically, Sharma's mutant *S. pombe* strain is one in which a synthetase involved in energy metabolism is inactivated. Sharma, however, does not describe is the deletion of at least one gene chosen from pyruvate decarboxylase, aspartic protease, serine protease, aminopeptidase, and carboxypeptidase as set forth in the claims. Therefore, the claims are not anticipated by the disclosure of this patent and as such withdrawal of this rejection is requested.

The IDS of February 2004 was a submission of an International Preliminary Examination Report for PCT/JP02/05223, the parent of the present application. As stated in this report, citing JP 2000-136199 and JP2000-262284:

> The subject matter of claims 1-13 appear to involve an inventive step in view of documents 1 and 2 cited in the ISR. Documents 1 and 2 do not describe that the genome part of the eukaryote host is deleted or inactivated to improve the

efficiency of production of foreign protein by a transformant of the eukaryote host. A person could not have easily conceived of it in view of documents 1 and 2.

If the Examiner deems further information related to this report is needed, Applicants request that he contact their undersigned US representative.

As for the required substitute Declaration, one is attached hereto along with a substitute Application Data Sheet to correct Mr. Tohda's name.

A Notice of Allowance for all pending claims is earnestly solicited.

Should the Examiner deem that any further action is necessary to place this application in even better form for allowance, he is encouraged to contact Applicants' undersigned representative.

Respectfully submitted,

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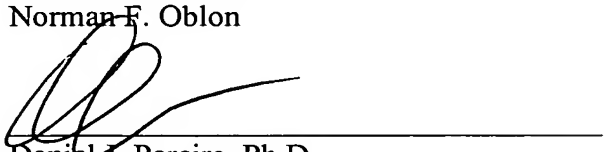
Norman F. Oblon



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